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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/584,455	09/20/2006	Sarman Singh	506816	4147

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EXAMINER	
WILDER, CYNTHIA B	

ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
01/09/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

RockMail@reinhartlaw.com

Office Action Summary	Application No.	Applicant(s)	
	10/584,455	SINGH ET AL.	
	Examiner	Art Unit	
	CYNTHIA B. WILDER	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed October 22, 2008 is acknowledged and has been entered. Claims 2-4, 12 and 14 have been amended. Claims 1-18 are pending. All of the arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

This action is made FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Once again claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Macklin et al (WO 0047227, August 2000) and Britton et al (2004035619, October 2002) in view of Buck et al (Biotechniques, vol. 27, pages 528-536, September 1999).

Regarding claim 1, Macklin et al teach an oligonucleotide primer pair for amplification Early Secretory Antigenic Target (*esat*)-6-gene of Mycobacterium species (pages 30-32). Macklin et al teach an *esat*-6 primer sequence that is substantially identical to the sequence of SEQ ID NO: 3 (see alignment below):

```
 SEQ ID NO: 3            9 CATGACAGAGCAGCAGTGGA 28
                           ||||||||||||||||||||
Macklin et al.           9 CATGACAGAGCAGCAGTGGA 28
```

Britton et al teach a composition and method useful in the treatment of diseases including infectious diseases and cancer. Britton teach a polynucleotide sequence encoding M. tuberculosis antigen *esat-6* (SEQ ID NO: 17) which comprises sequences that are 100% identical to the sequence of the SEQ ID NO: 3 and SEQ ID NO: 4 (see alignment below):

```
SEQ ID NO: 3             1 GCGGATCCCATGACAGAGCAGCAGTGGA 28
                           ||||||||||||||||||||||||||||
Britton et al.           5 GCGGATCCCATGACAGAGCAGCAGTGGA 32
(SEQ ID NO:17)
SEQ ID NO: 4           1 CCCAAGCTTCCTATGCGAACATCCCAGTGACG 32
                         ||||||||||||||||||||||||||||||||
Britton et al.       311 CCCAAGCTTCCTATGCGAACATCCCAGTGACG 280
(SEQ ID NO: 17)
```

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general

method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated, "Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound... Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed primers and probes simply represent structural homologs of the oligonucleotides taught by Macklin et al and Britton et al and which are derived from sequences expressly suggested by the prior art of and known in the prior art as disclosed the prior art as useful for primers for the detection of *M. tuberculosis* and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers and probes are *prima facie* obvious over the cited references in the absence of secondary considerations.

With regard to the issue of equivalence of the oliognucleotides, MPEP 2144.06 notes "Substituting equivalents known for the same purpose. In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. An express suggestion to substitute one equivalent component or process for another is

not necessary to render such substitution obvious. *In re Fout,* 675 F.2d 297, 213 USPQ 532 (CCPA 1982)."

With regard to the issue of reasonable expectation of success in using such equivalents, Buck et al expressly provides a general teaching of evidence of the equivalence of primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18-mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods of the different labs, Buck found that EVERY SINGLE PRIMER worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)."

Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95-control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every oligonucleotide would have a reasonable expectation of success.

9. Once again, claims 2-11 are rejected under 35 U.S.C. 103(a) as being unpatentable Young (EP 0 528 306, August 1992) in view of Macklin et al and Britton as previously applied above. Regarding claims 2, 5, 7, and 11, Young et al teach a method and kit for detecting *M. tuberculosis* in a sample, the said method comprising the steps of isolating DNA from the sample, amplifying the DNA template by adding a reaction, oligonucleotide primer pair, all four dNTPs, and heat stable DNA polymerase, wherein said polymerase is TAQ polymerase, to obtain an amplified DNA product, and subjecting the amplified DNA product of step (b) to separation, and staining to detect the presence of amplified DNA product wherein the presence of amplified DNA product is indicative of *M. tuberculosis* in the sample (page 30-43, page 7-8 and Example 2). Young further teaches positive and negatives control.

Young et al do not expressly teach wherein the detecting is based on the amplification of sequences from the esat-6 gene, using primers comprising the sequences of SEQ ID NOS: 3 and 4.

Macklin et al teach a PCR method and oligonucleotides used to amplify *M. tuberculosis*, wherein said method is based on amplification of the *esat-6* gene. Macklin teaches wherein one of the oligonucleotides used for amplifying *M. tuberculosis* is substantially identical to SEQ ID NO: 3 (pages 30-32) (see alignment below).

```
SEQ ID NO: 3          9 CATGACAGAGCAGCAGTGGA 28
                        ||||||||||||||||||||
Macklin et al.        9 CATGACAGAGCAGCAGTGGA 28
```

Macklin et al teaches that the esat-6 gene is specific for *M. tuberculosis* gene (see page 30).

Britton et al teach a composition and method useful in the treatment of diseases including infectious diseases and cancer. Britton teach a polynucleotide sequence encoding M. tuberculosis antigen *esat-6* (SEQ ID NO: 17) which comprises sequences that are 100% identical to the sequence of the SEQ ID NO: 3 and SEQ ID NO: 4 (see alignment below).

```
SEQ ID NO: 3              1 GCGGATCCCATGACAGAGCAGCAGTGGA 28
                            ||||||||||||||||||||||||||||
Britton et al.            5 GCGGATCCCATGACAGAGCAGCAGTGGA 32
(SEQ ID NO:17)

SEQ ID NO: 4              1 CCCAAGCTTCCTATGCGAACATCCCAGTGACG 32
                            ||||||||||||||||||||||||||||||||
Britton et al.          311 CCCAAGCTTCCTATGCGAACATCCCAGTGACG 280
(SEQ ID NO: 17)
```

Britton supports Macklin in teaching that the esat-6 gene is specific for *M. tuberculosis* (pages 15).

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated, "Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound... Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain

compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed primers and probes simply represent structural homologs of the oligonucleotides taught by Macklin et al and Britton et al and which are derived from sequences expressly suggested by the prior art of and known in the prior art as disclosed the prior art as useful for primers for the detection of *M. tuberculosis* and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers and probes are *prima facie* obvious over the cited references in the absence of secondary considerations.

Since the esat-6 gene is specific for *M. tuberculosis*, it would have been further obvious to one of ordinary skill in the art at the time of the claimed invention to target sequences specific for the esat-6 gene as taught by Macklin and Britton for use in the PCR methods of Young et al for the obvious benefit of identifying *M. tuberculosis* in a desired sample for detecting of a disease stated or condition.

Regarding claims 3 and 4, Young teaches wherein the clinical sample is comprised of cells, particularly peripheral blood lymphocytes (pages 8, line 18).

Regarding claims 6, 8, 9 and 10, these claims merely recite a plethora of conventional nucleic acid manipulation reagents and methodologies, as well as well as routine optimization or reaction components, concentrations, and parameters. Clearly such conventional and trivial modification and optimizations do not contribute towards patentability. Thus, one of ordinary skill in the art would have been motivated to modify the primary references in the manner of the claims to achieve the expected benefits, optimizations and/or expanded applications (see Young et al, pages 5-9, Examples 2

and 5, 6 and 7). It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods. Further, MPEP states "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller,* 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Once again, claims 12-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Young as previously cited above in view of Ecker et al (WO

2004052175, filing effective date December 2002) in view of Macklin et al and Britton as previously applied above.

Regarding claims 12 and 15, Young et al teach a method and kit for detecting *M. tuberculosis* in a sample, the said method comprising the steps of amplifying a 16s rRNA region from an isolated DNA sample using primer that is substantially identical to the sequence of SEQ ID NO: 2 (see alignment below) to obtain a first amplified product which is used as a positive control.

```
SEQ ID NO: 2          7 ACAGGCCACAAGGGA 21
                        ||||||||||||||
Young                14 ACAGGCCACAAGGGA 28
```

Young further teaches a further teach additional amplification by adding a reaction, genus specific primer pairs, all four dNTPs, and a heat stable DNA polymerase, wherein said polymerase is TAQ polymerase, to obtain an amplified DNA product, and subjecting the amplified DNA product of step to separation, and staining to detect the presence of amplified DNA product wherein the presence of amplified DNA product is indicative of *M. tuberculosis* in the sample (page 30-43, page 7-8 and Example 2).

Young does not expressly teach amplification of the 16s RNA region further comprising the use of SEQ ID NO: 1.

Ecker et al teach a method for the identification of pathogens in human and animal sample using PCR techniques. Ecker et al further teaches a primer sequence that is identical to the sequence of SEQ ID NO: 1 for detecting a bacterial 16s rRNA region (see alignment below).

```
SEQ ID NO: 1          1 GAGAGTTTGATCCTGGCTCAG 21
                        |||||||||||||||||||||
```

```
Ecker et al          1 GAGAGTTTGATCCTGGCTCAG 21
```

Neither Young nor Ecker teach wherein the method comprising amplification of the esat-6 gene using the primer pair comprising the sequence of SEQ ID NO: 3 and 4.

Macklin et al teach a PCR method and oligonucleotides used to amplify *M. tuberculosis*, wherein said method is based on amplification of the *esat-6* gene. Macklin teaches wherein one of the oligonucleotides used for amplifying *M. tuberculosis* is substantially identical to SEQ ID NO: 3 (pages 30-32) (see alignment below).

```
 SEQ ID NO: 3          9 CATGACAGAGCAGCAGTGGA 28
                         ||||||||||||||||||||
Macklin et al.         9 CATGACAGAGCAGCAGTGGA 28
```

Macklin et al teaches that the esat-6 gene is specific for *M. tuberculosis* gene (see page 30).

Britton et al teach a composition and method useful in the treatment of diseases including infectious diseases and cancer. Britton teach a polynucleotide sequence encoding M. tuberculosis antigen *esat-6* (SEQ ID NO: 17) which comprises sequences that are 100% identical to the sequence of the SEQ ID NO: 3 and SEQ ID NO: 4 (see alignment below).

```
SEQ ID NO: 3           1 GCGGATCCCATGACAGAGCAGCAGTGGA 28
                         ||||||||||||||||||||||||||||||
Britton et al.         5 GCGGATCCCATGACAGAGCAGCAGTGGA 32
(SEQ ID NO:17)

SEQ ID NO: 4           1 CCCAAGCTTCCTATGCGAACATCCCAGTGACG 32
                         ||||||||||||||||||||||||||||||||
Britton et al.       311 CCCAAGCTTCCTATGCGAACATCCCAGTGACG 280
(SEQ ID NO: 17)
```

Britton supports Macklin in teaching that the esat-6 gene is specific for *M. tuberculosis* (pages 15).

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated, "Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound... Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed primers and probes simply represent structural homologs of the oligonucleotides taught by Macklin et al and Britton et al and which are derived from sequences expressly suggested by the prior art of and known in the prior art as disclosed the prior art as useful for primers for the detection of *M. tuberculosis* and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers and probes are *prima facie* obvious over the cited references in the absence of secondary considerations.

Since the esat-6 gene is specific for *M. tuberculosis*, it would have been further obvious to one of ordinary skill in the art at the time of the claimed invention to target

sequences specific for the esat-6 gene as taught by Macklin and Britton for use in the PCR methods of Young et al for the obvious benefit of identifying *M. tuberculosis* in a desired sample for detecting of a disease stated or condition.

Regarding claims 13 and 14, Young teaches wherein the clinical sample is comprised of cells, particularly peripheral blood lymphocytes (pages 8, line 18).

Regarding claims 16-18, these claims merely recite a plethora of conventional nucleic acid manipulation reagents and methodologies, as well as well as routine optimization or reaction components, concentrations, and parameters. Clearly such conventional and trivial modification and optimizations do not contribute towards patentability. Thus, one of ordinary skill in the art would have been motivated to modify the primary references in the manner of the claims to achieve the expected benefits, optimizations and/or expanded applications (see Young et al, pages 5-9, Examples 2 and 5, 6 and 7). It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods. Further, MPEP states "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller,* 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Response to Arguments

13. Applicant traverse the rejection on the following grounds: Applicant states that Macklin et al provides a composition containing recombinant nucleic acid molecule which encode at least two M. tuberculosis antigens. Applicant states that nowhere in

the description does Macklin et al teach or provide any indication for identification of Mycobacterium tuberculosis. Applicant states the primer sequence cited by the Examiner and states that changes of a single nucleotide, alters the full function and scope of the sequence. Applicant provides a sequence alignment and states that as seen from the alignment, the sequences are substantially different. With regards to Britton et al, Applicant states that the sequences cited by Britton is the nucleotide sequence encoding M. tuberculosis antigen esat-6. Applicant states that the present inventions are expected to match a part of the whole gene sequence of esat-g gene as disclosed in Britton et al. Applicant states that Britton uses antigen antibody test methods that are unlike the present invention. Applicant states it would require undue experimentation for a person skilled in the art to come to the conclusion that Mycobacterium can be detected and even if such a conclusion is reached, he cannot differentiate between M. tuberculosis and M. Bovis. Applicant states that the present invention involves a thorough experimentation and analysis and has shown certain unexpected results, which were unexplored by anyone in the prior art. Applicant states that even though primers specific for Mycobacterium tuberculosis complex has been reported, it is first time that primes have been identified which can differentiate Mycobacterium tuberculosis from M. bovis based on ESAT-6 gene sequence. Applicant summarizes teachings from the specification and states that the present invention shows its utility in species specific and rapid molecular diagnosis of tuberculosis using esat-6 gene amplification, for the first time. Applicant states that therefore, even if the ESAT-6 gene sequence is disclosed in Britton et al and primer of

ESAT 6 gene is disclosed in Macklin et al, none of the two provide a method for identification of M. tuberculosis and further differentiate it with M. Bovis. Applicant states that more so it is not obvious to design a primer, knowing the whole sequence of the gene. Applicant states that an ordinary person in the prior art cannot be motivated to perform experiments to determine the genus and species specificity of primers of the ESAT gene. Applicant states that the Examiner cites Buck to discuss the equivalent of primers, however it is noted that without known the advantages of ESAT gene a person skilled in the art would not have an incentive to consider the use of ESAT over convention biochemical methods. Applicant states that none of the combined references teaches the invention of the claims 1-18.

14. All of the arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons that follow: In response to applicant's arguments concerning the rejections in view of Macklin and Britton and further in view of Buck, the Examiner maintains that the combination of cited prior arts provide direct evidence that there *exist* a reasonable expectation of success in designing oligonucleotides to known sequences to function as primers. As noted in the prior Office action, the prior art of Macklin et al provides oligonucleotide sequences substantially identical to the sequences of the instant invention for use as amplification primers in polymerase chain reactions (see for example pages 30-31). Macklin provides programs, e.g., BLAST and FASTA, which allows one to determine sequence percent identity for designing probes and primers (see pages 9, 11 and 12). Britton et al teaches oligonucleotide sequences that may be used as primer or probes in amplification type reactions. Britton also

teaches that the polynucleotide sequences of the invention may be aligned and percentages of identical nucleotides in specified regions may be determined against another polynucleotide using computer algorithms that are publicly available, such as BAST and FASTA (see pages 11 and 12).

Further, contrary to Applicant's arguments, it is noted that designing primers and probes which are equivalent to those taught in the art is routine experimentation. Routine optimization is not considered inventive and no evidence has been presented that the design of the primers as claimed was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

Likewise, the prior art teaches parameters and objectives involved in the selection of oligonucleotides that function as probes and primers (see e.g., Macklin, Britton and Buck et al). Likewise, the art teaches parameters for aligning sequences for proper selection of primers and probes, thus supporting routine experimentation (see for e.g., Elinifro et al., Clinical Microbiology Reviews, vol. 13, no. 4, pages 559-570, Oct. 2000). The arts are replete with guidance and information necessary to permit the ordinary artisan in the field of nucleic acid detection to routinely design primers and probes as well as specifically exemplifying that such methods work albeit with different primer sequences. The Examiner noted that the ordinary artisan would have had a reasonable expectation of success of obtaining primers and probes from the sequences taught by Macklin et al and Britton et al and Buck et al. The arguments above are also pertinent to the rejections in view of Young et al and Ecker et al.

With regard to the assertions of surprising and unexpected results in the specification, it is noted that the arguments of counsel cannot take the place of evidence in the record (*In re Schulze,* 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965)). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant (see MPEP 716.01 (b)). Applicant's arguments are not sufficient to overcome the prior art rejections above. Accordingly, the prior art rejections noted above are maintained.

Conclusion

15. No claims are allowed. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CYNTHIA B. WILDER whose telephone number is (571)272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/GARY BENZION/
Supervisory Patent Examiner, Art Unit 1637